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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/753,313	12/29/2000	Gerardo Castillo	PROTEO.P16	1184

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EXAMINER	
TATE, CHRISTOPHER ROBIN	
ART UNIT	**PAPER NUMBER**
1655	

DATE MAILED: 01/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/753,313	CASTILLO ET AL.	
	Examiner	Art Unit	
	Christopher R. Tate	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,5,10 and 28-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,5,10 and 28-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 14 November 2005 has been entered.

Claims 4, 5, 10, and 28-32 have been examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 4, 5, 10, and 28-32 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons set forth in the previous Office action which are restated below.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The newly recited claim limitations "such that it is the therapeutic amount of the substance administered that treats or disrupts the amyloid fibrils" (claims 4, 28, and 31) and "produced by process have the steps of (1) water extraction, using water that is not boiling" (claim 31) are deemed new matter as no literal support for these limitations were found in the instant disclosure.

Applicants' arguments concerning the above rejection have been carefully considered but are not deemed to be persuasive of error in the rejection. Applicants argue that Example I of the instant specification recites "extracted in 1 ml of distilled water" and, thus, persons of skill in the art would take this statement in the context of its attendant disclosure to mean that the water was not boiling, else it would have been so specified. However, as previously discussed, the specification does not preclude the use of boiling water and, thus, this negative limitation is still considered to be new matter. Applicants further argue that the entire thrust of the disclosure is directed to amyloid inhibition by administering the therapeutic amount of substance. However, amyloid inhibition does not necessarily or directly correlate to providing the limitation "such that it is the therapeutic amount of the substance administered that treats or disrupts the amyloid fibrils" and, thus, this limitation is still deemed to be new matter.

Claim Rejections - 35 USC § 102

Claims 4, 5, and 28-31 stand rejected under 35 U.S.C. 102(b) as being anticipated by Mitsui Norin (JP 10-245342), or by Takami et al. (JP 10-175858) for the reasons set forth in the previous Office action which are restated and expanded upon below.

Mitsui Norin teaches the administration (e.g., in oral dosage form) of a therapeutically effective amount of epicatechin (which is a naturally occurring compound extracted from green tea and, thus, reads upon a green tea extract) as well as green tea extract (per se), to a subject suffering from Alzheimer's disease so as to inhibit senile plaque formation due to the deposition of beta-amyloid protein on brain nerve cells and, thus, reduce the toxicity of beta-amyloid

protein (see entire English translation of this JP patent) - please note that beta-amyloid protein is medically well known to be responsible for amyloid fibril formation, deposition, accumulation, aggregation, and/or persistence. [Further, as previously discussed, Applicants readily admit that "Alzheimer's disease is characterized by the accumulation of ... beta-amyloid protein or A*B*, in a fibrillar form, existing as extracellular amyloid plaques and as amyloid with the wall of cerebral blood vessels. Fibrillar A*B* amyloid deposition in Alzheimer's disease is believed to be detrimental to the patient and eventually leads to toxicity and neuronal cell death characteristic hallmarks of Alzheimer's disease. Accumulating evidence implicates amyloid as a major causative factor of Alzheimer's disease pathogenesis" - see page 1, lines 12-18 of the instant specification - accordingly, the claimed functional effect would inherently occur upon the oral administration of an effective amount of green tea extract, as taught by the cited reference.]

Takami et al. teach the administration (e.g., in the form of a pharmaceutical tablet, capsule, etc; or within a consumable drink or food, etc) of a pharmacologically effective amount of a green tea extract (which is produced via warm or hot water extraction; e.g., TEAFURAN 30) containing epicatechin therein, or a component thereof - such as epicatechin, including to someone suffering from Alzheimer's disease brought about by toxicity of beta amyloid protein. See entire computer-generated English translation of the JP patent. Please again note that claimed functional effect would inherently occur upon the oral administration of an effective amount of green tea extract, as taught by the cited reference. Please also note that such an amount would inherently be in an amount to provide the claimed functional effect.

It is reemphasized that the above reference methods would inherently provide the functional effects instant claimed - i.e., would inherently treat/disrupt amyloid fibril formation,

deposition, accumulation, aggregation, and/or persistence in a subject suffering from Alzheimer's disease upon oral consumption of a therapeutically effective amount such a green tea extract since amyloid fibril formation, deposition, accumulation, aggregation and/or persistence is inherently present in Alzheimer's patients (see, e.g., page 1, lines 12-18 of the instant specification - as discussed above; in addition, also see the review article by Selkoe including, e.g., page 743 under the heading *Neuritic Plaques* with respect to the inherent presence of amyloid fibrils in Alzheimer's patients).

Therefore, each of the cited references is deemed to anticipate the instant claims above.

Claim Rejections - 35 USC § 103

Claims 4, 5, 10, and 28-32 stand/are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitsui Norin and Takami et al. (JP 10-175858), in view of Chatterjee et al. (US 4,892,883) and the admitted state of the art for the reasons set forth in the previous Office action which are restated and expanded upon below.

The primary references are relied upon for the reasons discussed *supra*. Neither of these references expressly teach the further inclusion of the herbal agents instantly recited in claim 10.

Chatterjee et al. beneficially disclose that administration of *Ginkgo biloba* is useful in the therapy of Alzheimer's disease (see, e.g., col 7, lines 13-39).

It would have been obvious to employ a therapeutically effective amount of green tea extract - such as beneficially taught by Mitsui Norin and Takami et al., for administering to a subject suffering from Alzheimer's disease so as to inhibit senile plaque formation due to the deposition of beta-amyloid protein on brain nerve cells based upon the beneficial teachings

provided therein. [As noted above and in previous Office actions, the reference methods would intrinsically provide the functional effects instant claimed - i.e., would intrinsically treat/disrupt amyloid fibril formation, deposition, accumulation, aggregation, and/or persistence in a subject suffering from Alzheimer's disease upon such oral consumption.]

It would also have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine (and orally administer) green tea extract with *Ginkgo biloba* (for treating Alzheimer's disease) for the following reasons. It is well known that it is *prima facie* obvious to combine two or more ingredients each of which is beneficially taught to be useful for the same purpose (e.g., treating Alzheimer's disease) in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. In re Sussman, 1943 C.D. 518; In re Pinten, 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); In re Susi, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicants' arguments concerning the above art rejections have been carefully considered but are not deemed to be persuasive of error in the rejections. Applicants argue that the

Examiner is implying that beta-amyloid nerve toxicity, or reduction of active oxygen, necessarily (that is, 'inherently') teaches an effect on the treatment of beta-amyloid plaque formation; and also that there are thus no necessary inferences to be drawn from the cited studies pertaining to neuronal cell death or active oxygen reduction as to *AB* fibrillogenesis. However, these arguments are not deemed persuasive given the fact that treating the instantly claimed functional effect (i.e., treating beta amyloid fibril formation/deposits/aggregation/persistence) would inherently occur upon oral administration of such green tea extracts since amyloid fibril formations/deposits are inherently present Alzheimer's patients - thus, the treatment and/or disruption of amyloid fibril formations/deposits/aggregations/persistence would inherently occur upon oral administration of the prior art green tea extracts to a subject suffering from Alzheimer's disease - in which beta-amyloid fibril formations, depositions, aggregations, and/or persistence would inherently be present - i.e., they would already inherently exist in a subject suffering from Alzheimer's disease (as further evidence - see, e.g., the entire review article by Selkoe including, e.g., page 743 under the heading *Neuritic Plaques*, as well as the admitted state of the art - see page 1, lines 12-18 of the instant specification, with respect to such inherency as discussed *supra* - including the art-recognized fact that such amyloid fibrils would already exist in a patient suffering from Alzheimer's disease). Otherwise, as discussed in the previous Office action, the instant invention would not work as claimed/disclosed since beta-amyloid fibril formations, deposits, accumulations, aggregations, and/or persistence are inherently present in a subject suffering from Alzheimer's disease. In other words, Applicants appear to be arguing patentability based upon discovering (and claiming) an underlying functional effect concerning how green tea extract works with respect to treating a subject suffering from Alzheimer's disease.

However, as discussed above, this underlying functional effect (i.e., treating/disrupting amyloid fibril formation, deposition, aggregation, and/or persistence) would intrinsically occur in an Alzheimer's patient being administered such a green tea extract - including those disclosed by the cited prior art references.

Applicants also argue that instant claim 31 (drawn to a method of using a product-by-process) requires that that the green tea extract be created by water extraction using water that is not boiling as well as removal of the fluid supernatant therefrom. However, as previously discussed, with respect to the instantly claimed method of using a product-by-process (e.g., claim 31), please note that in product-by-process claims (including methods of using a product-by-process), "once a product appearing to be substantially identical is found and a 35 U.S.C. 102 and/or 103 rejection [is] made, the burden shifts to the applicant to show an unobvious difference." MPEP 2113. Applicants have failed to objectively show an unobvious difference between the reference green tea extract products and the claimed green tea extract product (including that used within the method of instant claim 31). That is, other than arguing that the Mitsui Norin reference uses boiling water (which is then separated) and, thus, is prepared by a different process that that recited in instant claim 31, no objective evidence has been provided to show an unobvious difference between the Mitsui Norin green tea extract and the green tea extract of claim 31. In addition, it should be noted that the Takami et al. reference expressly teaches that their water extract can be prepared via warm (thus, not boiling) or hot water extraction (paragraph [0010]) and then dried (which would inherently separate the supernatant therefrom). Accordingly, the therapeutic green tea extract preparation disclosed by Takami et al. is still deemed to read upon the green tea extract product-by-process of instant claim 31.

Applicants further argue that claim 10 properly reads upon claim 4 and as such, all cited references fail to suggest the combination of steps and substances actually claimed, and that they traverse the Examiner's unsupported supposition that any of the listed ingredients (recited in claim 10) are known in the art to be efficacious in treating amyloid fibrils. In response, the Examiner would like to again point out it appeared to him, based upon the teachings of the instant specification, that the ingredients recited in instant claim 10 are admittedly well known in the art to function as such since none of the herbal agents recited in claim 10 were actually tested in the instant Examples, and page 6, lines 14-20 of the instant specification merely states that they are amyloid inhibitory ingredients. Regardless, Chatterjee et al. beneficially disclose that administration of *Ginkgo biloba* is useful in the therapy of Alzheimer's disease (see, e.g., col 7, lines 13-39). Accordingly, the USC 103 rejection with respect to claim 10 is deemed proper because, as discussed above, it is well known to be *prima facie* obvious to combine two or more ingredients each of which is beneficially taught to be useful for the same purpose - i.e., treating Alzheimer's disease, in order to form a third composition which is useful for the same purpose (as well as to actually use such a combination to treat Alzheimer's disease in a subject) - for the reasons fully set forth above under USC 103.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher R. Tate whose telephone number is (571) 272-0970. The examiner can normally be reached on Mon-Thur, 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher R. Tate
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Art Unit 1655